10/539,544
Search Hcook 7/11/07

d his

(FILE 'HOME' ENTERED AT 11:32:55 ON 11 JUL 2007)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, JAPIO' ENTERED AT 11:33:16 ON 11 JUL 2007

L1	33564	S	(INOSITOL PHOSPHATE)
L2	84	S	L1 AND (METAL ION)
L3	68	S	L2 AND PD<2004
L4	37		DUPLICATE REMOVE L3 (31 DUPLICATES REMOVED)
L5	1	S	L4 AND SCINT?
L6	1	S	L4 AND BEAD?
L7	0	S	L6 NOT L5
L8	3	S	L4 AND ASSAY?

=>

```
d his

     (FILE 'HOME' ENTERED AT 11:32:55 ON 11 JUL 2007)

     FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, JAPIO' ENTERED AT 11:33:16 ON 11
     JUL 2007
L1         33564 S (INOSITOL PHOSPHATE)
L2            84 S L1 AND (METAL ION)
L3            68 S L2 AND PD<2004
L4            37 DUPLICATE REMOVE L3 (31 DUPLICATES REMOVED)
L5             1 S L4 AND SCINT?
L6             1 S L4 AND BEAD?
L7             0 S L6 NOT L5
L8             3 S L4 AND ASSAY?

=>
```

ANSWER 2 OF 3 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

AN 1999058882 EMBASE

TI Action of phosphatidylinositol-specific phospholipase Cγ1 on soluble and micellar substrates: Separating effects on catalysis from modulation of the surface.

AU Zhou C.; Horstman D.; Carpenter G.; Roberts M.F.

CS M.F. Roberts, Merkert Chemistry Center, Boston College, Chestnut Hill, MA 02467, United States. mary.roberts@bc.edu

SO Journal of Biological Chemistry, (29 Jan 1999) Vol. 274, No. 5, pp. 2786-2793. .
Refs: 32
ISSN: 0021-9258 CODEN: JBCHA3

CY United States

DT Journal; Article

FS 029 Clinical Biochemistry

LA English

SL English

ED Entered STN: 19 Mar 1999
Last Updated on STN: 19 Mar 1999

AB The kinetics of PI-PLCγ1 toward a water-soluble substrate (inositol 1,2-cyclic phosphate, cIP) and phosphatidylinositol (PI) in detergent mixed micelles were monitored by sip NMR spectroscopy. That cIP is also a substrate (K(m) = .apprx. 15 mM) implies a two-step mechanism (intramolecular phosphotransferase reaction to form cIP followed by cyclic phosphodiesterase activity to form inositol-1-phosphate (I-1-P)). PI is cleaved by PI-PLCγ1 to form cIP and I-1-P with the enzyme specific activity and ratio of products (cIP/I-1-P) regulated by assay temperature, pH, Ca2+, and other amphiphilic additives. Cleavage of both cIP and PI by the enzyme is optimal at pH 5. The effect of Ca2+ on PI-PLCγ1 activity is unique compared with other isozymes enzymes: Ca2+ is necessary for the activity and low Ca2+ activates the enzyme; however, high Ca2+ inhibits PI-PLCγ1 hydrolysis of phosphoinositides (but not cIP) with the extent of inhibition dependent on pH, substrate identity (cIP or PI), substrate presentation (e.g. detergent matrix), and substrate surface concentration. This inhibition of PI-PLCγ1 by high Ca2+ is proposed to derive from the divalent metal ion-inducing clustering of the PI and reducing its accessibility to the enzyme. Amphiphilic additives such as phosphatidic acid, fatty acid, and sodium dodecylsulfate enhance PI cleavage in micelles at pH 7.5 but not at pH 5.0; they have no effect on cIP hydrolysis at either pH value. These different kinetic patterns are used to propose a model for regulation of the enzyme. A key hypothesis is that there is a pH-dependent conformational change in the enzyme that controls accessibility of the active site to both water-soluble cIP and interfacially organized PI. The low activity enzyme at pH 7.5 can be activated by PA (or phosphorylation by tyrosine kinase). However, this activation requires lipophilic substrate (PI) present because cIP hydrolysis is not enhanced in the presence of PA.

CT Medical Descriptors:
*catalysis
*enzyme kinetics
micelle
phosphorus nuclear magnetic resonance
enzyme activity
temperature
pH
enzyme substrate
conformational transition
enzyme active site
enzyme activation
hydrolysis
nonhuman
rat

controlled study
article
priority journal
Drug Descriptors:
*phosphatidylinositol
*phospholipase c: EC, endogenous compound
inositol 1,2 cyclic phosphate
inositol phosphate
phosphodiesterase
calcium ion
phosphatidic acid
fatty acid
dodecyl sulfate
RN (phospholipase c) 9001-86-9; (inositol 1,2 cyclic phosphate) 43119-57-9; (inositol phosphate) 15421-51-9; (calcium ion) 14127-61-8; (dodecyl sulfate) 151-41-7

ANSWER 2 OF 3 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

AN 1999058882 EMBASE

TI Action of phosphatidylinositol-specific phospholipase Cγ1 on soluble and micellar substrates: Separating effects on catalysis from modulation of the surface.

AU Zhou C.; Horstman D.; Carpenter G.; Roberts M.F.

CS M.F. Roberts, Merkert Chemistry Center, Boston College, Chestnut Hill, MA 02467, United States. mary.roberts@bc.edu

SO Journal of Biological Chemistry, (29 Jan 1999) Vol. 274, No. 5, pp. 2786-2793. .
Refs: 32
ISSN: 0021-9258 CODEN: JBCHA3

CY United States

DT Journal; Article

FS 029 Clinical Biochemistry

LA English

SL English

ED Entered STN: 19 Mar 1999
Last Updated on STN: 19 Mar 1999

AB The kinetics of PI-PLCγ1 toward a water-soluble substrate (inositol 1,2-cyclic phosphate, cIP) and phosphatidylinositol (PI) in detergent mixed micelles were monitored by sip NMR spectroscopy. That cIP is also a substrate (K(m) = .apprx. 15 mM) implies a two-step mechanism (intramolecular phosphotransferase reaction to form cIP followed by cyclic phosphodiesterase activity to form inositol-1-phosphate (I-1-P)). PI is cleaved by PI-PLCγ1 to form cIP and I-1-P with the enzyme specific activity and ratio of products (cIP/I-1-P) regulated by assay temperature, pH, Ca2+, and other amphiphilic additives. Cleavage of both cIP and PI by the enzyme is optimal at pH 5. The effect of Ca2+ on PI-PLCγ1 activity is unique compared with other isozymes enzymes: Ca2+ is necessary for the activity and low Ca2+ activates the enzyme; however, high Ca2+ inhibits PI-PLCγ1 hydrolysis of phosphoinositides (but not cIP) with the extent of inhibition dependent on pH, substrate identity (cIP or PI), substrate presentation (e.g. detergent matrix), and substrate surface concentration. This inhibition of PI-PLCγ1 by high Ca2+ is proposed to derive from the divalent metal ion-inducing clustering of the PI and reducing its accessibility to the enzyme. Amphiphilic additives such as phosphatidic acid, fatty acid, and sodium dodecylsulfate enhance PI cleavage in micelles at pH 7.5 but not at pH 5.0; they have no effect on cIP hydrolysis at either pH value. These different kinetic patterns are used to propose a model for regulation of the enzyme. A key hypothesis is that there is a pH-dependent conformational change in the enzyme that controls accessibility of the active site to both water-soluble cIP and interfacially organized PI. The low activity enzyme at pH 7.5 can be activated by PA (or phosphorylation by tyrosine kinase). However, this activation requires lipophilic substrate (PI) present because cIP hydrolysis is not enhanced in the presence of PA.

CT Medical Descriptors:
*catalysis
*enzyme kinetics
micelle
phosphorus nuclear magnetic resonance
enzyme activity
temperature
pH
enzyme substrate
conformational transition
enzyme active site
enzyme activation
hydrolysis
nonhuman
rat

controlled study
article
priority journal
Drug Descriptors:
*phosphatidylinositol
*phospholipase c: EC, endogenous compound
inositol 1,2 cyclic phosphate
  inositol phosphate
phosphodiesterase
calcium ion
phosphatidic acid
fatty acid
dodecyl sulfate
RN (phospholipase c) 9001-86-9; (inositol 1,2 cyclic phosphate) 43119-57-9; (inositol phosphate) 15421-51-9; (calcium ion) 14127-61-8; (dodecyl sulfate) 151-41-7

10/539,544
Yoder 7/11/07

d his

(FILE 'HOME' ENTERED AT 11:32:55 ON 11 JUL 2007)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, JAPIO' ENTERED AT 11:33:16 ON 11 JUL 2007

L1	33564	S (INOSITOL PHOSPHATE)
L2	84	S L1 AND (METAL ION)
L3	68	S L2 AND PD<2004
L4	37	DUPLICATE REMOVE L3 (31 DUPLICATES REMOVED)
L5	1	S L4 AND SCINT?
L6	1	S L4 AND BEAD?
L7	0	S L6 NOT L5
L8	3	S L4 AND ASSAY?
L9	2	S L1 AND ZR4?
L10	93	S L1 AND F3?
L11	17	S L1 AND FE3?
L12	11	DUPLICATE REMOVE L11 (6 DUPLICATES REMOVED)
L13	10	S L12 AND PD<2004

d his

(FILE 'HOME' ENTERED AT 11:32:55 ON 11 JUL 2007)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, JAPIO' ENTERED AT 11:33:16 ON 11 JUL 2007

L1	33564	S (INOSITOL PHOSPHATE)
L2	84	S L1 AND (METAL ION)
L3	68	S L2 AND PD<2004
L4	37	DUPLICATE REMOVE L3 (31 DUPLICATES REMOVED)
L5	1	S L4 AND SCINT?
L6	1	S L4 AND BEAD?
L7	0	S L6 NOT L5
L8	3	S L4 AND ASSAY?
L9	2	S L1 AND ZR4?
L10	93	S L1 AND F3?
L11	17	S L1 AND FE3?
L12	11	DUPLICATE REMOVE L11 (6 DUPLICATES REMOVED)
L13	10	S L12 AND PD<2004

ANSWER 5 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1989:493130 CAPLUS
DN 111:93130
ED Entered STN: 16 Sep 1989
TI HPLC separation and detection of inositol phosphate isomers
AU Henderson, Susan K.; Desplaines, Kimberly; Henderson, David E.
CS Dep. Chem., Quinnipiac Coll., Hamden, CT, 06518, USA
SO BioChromatography (1989), 4(2), 89-93
CODEN: BCHREF; ISSN: 0888-4404
DT Journal
LA English
CC 9-3 (Biochemical Methods)
AB The use of metal ions, Fe3+, Zn2+, tris(2,2,6,6-tetramethyl-3,5-heptanedionato)europium(III) [Eu(DPM)3], and ferroin, as mobile phase additives to enhance the UV detection of inositol phosphate isomers was investigated. Spectrophotometric studies of myo-inositol phosphate with FeCl3 were performed, and it was concluded that an Fe3+/myo-inositol-phosphate complex formed with a UV absorption maximum at 280 nm. For the addnl. two metal ions, Zn2+ and Fe2+, and for ferroin, it was concluded that their presence in the mobile phase did not result in changes in absorbance that would enhance the UV detection of the inositol phosphate compds. The addition of Eu(DPM)3 allowed detection but did not yield the sensitivity of Fe3+. Myo-inositol-2-monophosphate (IMP) was separated on a reverse-phase HPLC column using a formate buffer containing FeCl3 and an iron pairing reagent, tetrabutylammoniumhydroxide. Addition of Fe3+ to the mobile phase allowed quant. determination of myo-inositol-2-monophosphate over a range extending from 20-500 ng by absorption at 280 nm. Estimated detection limits were .apprx.15-20 ng. Separation of phytic acid (PY) and other inositol phosphate isomers have not yet been reliably achieved under these conditions.
ST inositol phosphate isomer sepn detection; HPLC inositol phosphate UV spectrometry; liq chromatog inositol phosphate
IT Spectrochemical analysis
(UV, for inositol phosphate isomers, after HPLC)
IT Chromatography, column and liquid
(high-performance, of inositol phosphate isomers)
IT 7439-89-6, Iron, uses and miscellaneous
RL: USES (Uses)
(in inositol phosphate spectrophotometric determination)
IT 131-99-7, IMP 132-06-9, ITP 7336-80-3 68247-19-8D, Inositol phosphate, isomers
RL: ANST (Analytical study)
(separation and detection of, by HPLC)